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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SASAN, ARADHANA	
ART UNIT	PAPER NUMBER
1615	
MAIL DATE	DELIVERY MODE
11/10/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/530,785	NONOMURA ET AL.	
	Examiner	Art Unit	
	ARADHANA SASAN	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 August 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/24/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. The remarks, amendments, and Request for Continued Examination filed on 08/24/09 are acknowledged.

2. Claims 1-22 were cancelled. New claims 27-31 were added.

3. Claims 23-31 are included in the prosecution.

Information Disclosure Statement

4. The information disclosure statement (IDS) submitted on 08/24/09 is acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97 and 1.98. Accordingly, the examiner is considering the information disclosure statement.

See attached copy of PTO-1449.

Continued Examination under 37 CFR 1.114

5. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 08/24/09 has been entered.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 23-26 **remain** rejected and new claims 27-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hashimoto et al. (WO 02/44167).

The claimed invention is a process for producing an amorphous optically active isomer of lansoprazole which comprises keeping hydrated crystals of optically active isomer (R-isomer) of lansoprazole at about 20 to about 100°C for a time sufficient to produce the amorphous optically active isomer of lansoprazole.

Hashimoto teaches a method of producing (R)-lansoprazole (Abstract). The (R) - lansoprazole produced by the method may be a crystal of (R)-lansoprazole and may be a hydrate. “The "hydrate” includes 0.5 hydrate to 5.0 hydrate. More preferred is 0.5 hydrate, 1.0 hydrate and 1.5 hydrate” (Page 8, lines 15-23). “The thus-obtained crystal may be used as it is, or dried … The "drying" includes, for example, vacuum drying, through-flow drying, drying by heating, air drying and the like” (Page 14, lines 1-5).

Hashimoto does not expressly teach the process of drying the hydrate of (R)-lansoprazole in the temperature range of about 20 to about 100°C.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the method of producing and drying a hydrate of (R)-lansoprazole, as taught by Hashimoto, and perform the drying at a temperature range of about 20 to about 100°C during the process of routine experimentation, and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because during the process of routine experimentation one would store the (R)-lansoprazole at room temperature or would dry the (R)-lansoprazole, which would lead to the formation of an amorphous (R)-lansoprazole.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Regarding instant claim 23, the process for producing an amorphous optically active isomer of lansoprazole which comprises keeping hydrated crystals of optically active isomer (R-isomer) of lansoprazole at about 20 to about 100°C would have been obvious over the method of producing and drying a hydrate of (R)-lansoprazole, as taught by Hashimoto (Page 8, lines 15-23 and Page 14, lines 1-5).

Regarding instant claim 24, the limitation of heating at about 40 to about 80°C would have been obvious over the method of drying a hydrate of (R)-lansoprazole, as taught by Hashimoto (Page 14, lines 1-5). One with ordinary skill in the art would modify the storage or drying temperature of a hydrate of (R)-lansoprazole during the process of routine experimentation and the recited temperature range would have been an obvious variant unless there is evidence of criticality or unexpected results.

Regarding instant claim 25, the limitation of 0.5 to 1.5 hydrate crystals of (R)-lansoprazole would have been obvious over the 0.5 hydrate, 1.0 hydrate and 1.5 hydrate taught by Hashimoto (Page 8, lines 15-23).

Regarding instant claim 26, the limitation of the keeping of the temperature under reduced pressure or under ventilation would have been obvious over the vacuum drying, through-flow drying, drying by heating, and air drying taught by Hashimoto (Page 14, lines 1-5).

Regarding instant claim 27, the limitation of the amorphous optically active isomer of lansoprazole that does not show a specific peak under an X-ray powder diffraction analysis would have been obvious over the amorphous lansoprazole isomer taught by Hashimoto (Page 8, lines 15-17). One of ordinary skill in the art would find analyzing the resultant lansoprazole isomer under X-ray powder diffraction obvious. Since the amorphous lansoprazole isomer is rendered obvious by Hashimoto, the property associated with the amorphous lansoprazole isomer (i.e., not showing a specific peak under an X-ray powder diffraction analysis) would have been obvious. Please see MPEP 2112.01. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present.

Regarding instant claims 28-29, the limitation of the hydrated crystals that show a specific peak under an X-ray powder diffraction analysis would have been obvious over the hydrated crystals taught by Hashimoto (Page 8, lines 18-19). One of ordinary skill in the art would find analyzing the resultant hydrated crystal of (R)-lansoprazole under X-

ray powder diffraction obvious. Since the hydrated crystal of (R)-lansoprazole is rendered obvious by Hashimoto, the property associated with the hydrated crystal of (R)-lansoprazole (i.e., showing a specific peak under an X-ray powder diffraction analysis) would have been obvious. Please see MPEP 2112.01. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. The limitation of drying the hydrated crystals at about 60ºC-70 ºC would have been obvious over the method of producing and drying a hydrate of (R)-lansoprazole, as taught by Hashimoto (Page 8, lines 15-23 and Page 14, lines 1-5).

Regarding instant claims 30-31, the limitation of the amorphous optically active isomer of lansoprazole that contains more amorphous form than crystalline form would have been obvious over the amorphous (R)-lansoprazole and the hydrated crystal of (R)-lansoprazole taught by Hashimoto (Page 8, lines 15-23 and Page 14, lines 1-5). One of ordinary skill in the art would find it obvious to modify the drying steps to increase crystalline lansoprazole or increase the amorphous lansoprazole formation.

Response to Arguments

8. Applicant's arguments, see Page 4, filed 08/24/09, with respect to the rejection of claims 23-26 under 35 USC § 103(a) as being unpatentable over Hashimoto et al. (WO 02/44167) have been fully considered but are not persuasive.

Applicant argues that "Hashimoto merely mentions only once in the entire disclosure that the starting material may be a solid that is amorphous, and fails to provide any reason to expect that an amorphous optically active isomer of lansoprazole

could be produced from hydrated crystals of optically active isomer (R-isomer) of lansoprazole. In fact, Hashimoto suggests just the opposite. In particular, Hashimoto teaches that the solid described on page g, lines 15-23, which may be crystal or amorphous, is obtained from a racemic mixture, as opposed to hydrated crystals of optically active isomer (R-isomer) of lansoprazole."

Applicant argues that "although Hashimoto teaches that the hydrated crystal is dried during the recrystallization process (page 14, line 25), Hashimoto clearly indicates that the product obtained at the end of this drying process is a crystal exhibiting specific peaks under X-ray powder diffraction analysis (page 14, line 28 to page 15, line 10). Thus, it is clear from this description that Hashimoto teaches that a solid can be obtained from a racemic mixture, that this solid can be amorphous or a crystal that is a hydrate, and this solid can be converted into a crystal exhibiting specific peaks under X-ray powder diffraction analysis, Nothing in Hashimoto indicates that the crystalline solid is converted into an amorphous optically active isomer. In fact, the reference teaches just the opposite to that of claim 23; that is, the reference teaches that after drying the amorphous solid, crystals exhibiting specific peaks under X-ray powder diffraction analysis are obtained."

Applicant argues that no water is introduced during the crystallization step and that the separated crystal obtained after partitioning and crystallizing is not a hydrated crystal, and as such, this crystal does not correspond to the hydrated crystal of claim 23. Applicant argues that nothing in Hashimoto indicates that the partitioned and crystallized crystal can be a hydrated crystal.

This is not persuasive because Hashimoto teaches that the (R)-lansoprazole produced is amorphous (Page 8, lines 15-23). Hashimoto also teaches that a crystal of (R)-lansoprazole that may be a hydrate is produced (Page 3, lines 15-23) and that the crystal that is obtained may be dried by vacuum drying, through-flow drying, drying by heating, air drying etc. (Page 14, lines 1-5). Therefore, the claimed elements of the process of producing an amorphous optically active isomer of lansoprazole are disclosed by Hashimoto and one of ordinary skill in the art would perform the drying step (of the hydrate) at various temperature ranges during the process of routine experimentation with a reasonable expectation of producing an amorphous optically active isomer of lansoprazole.

Therefore, the rejection of 12/22/08 is maintained.

Claim Rejections - 35 USC § 103

9. Claims 23-26 **remain** rejected and new claims 27-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fujishima et al. (WO 00/78745).

Fujishima teaches isolation of (R)-2-[[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridinyl]methyl]sulfinyl]-1H-benzimidazole (R(+)-lansoprazole) where the filtrate was evaporated to dryness to yield R(+)-lansoprazole as an amorphous substance (Page 13, line 30 to Page 14, line 16). The starting material is a crystal of R(+)-lansoprazole which may be a hydrate (Page 2, lines 32-34). The hydrate may be a 0.5 hydrate to 5.0 hydrate (Page 2, line 35 to Page 3, line 3).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the method of evaporating a hydrate of R(+)-lansoprazole to

dryness, as taught by Fujishima, and perform the drying at a temperature range of about 20 to about 100°C during the process of routine experimentation, and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because during the process of routine experimentation one would store the (R)-lansoprazole at room temperature or would dry the (R)-lansoprazole, which would lead to the formation of an amorphous (R)-lansoprazole.

Regarding instant claim 23, the process for producing an amorphous optically active isomer of lansoprazole which comprises keeping hydrated crystals of optically active isomer (R-isomer) of lansoprazole at about 20 to about 100°C would have been obvious over the method of evaporating to dryness a hydrate of R(+)-lansoprazole, as taught by Fujishima (Page 13, line 30 to Page 14, line 16, Page 2, lines 32-34).

Regarding instant claim 24, the limitation of heating at about 40 to about 80°C would have been obvious over the method of evaporating to dryness a hydrate of R(+)-lansoprazole, as taught by Fujishima (Page 13, line 30 to Page 14, line 16). One with ordinary skill in the art would modify the storage or drying temperature of a hydrate of (R)-lansoprazole during the process of routine experimentation and the recited temperature range would have been an obvious variant unless there is evidence of criticality or unexpected results.

Regarding instant claim 25, the limitation of 0.5 to 1.5 hydrate crystals of (R)-lansoprazole would have been obvious over the 0.5 hydrate, 1.0 hydrate and 1.5 hydrate taught by Fujishima (Page 2, line 35 to Page 3, line 3).

Regarding instant claim 26, the limitation of the keeping of the temperature under reduced pressure or under ventilation would have been obvious over the evaporating to dryness taught by Fujishima (Page 13, line 30 to Page 14, line 16). One of ordinary skill in the art would use the available methods of drying during the process of routine experimentation, including evaporation or air drying, drying by increasing the temperature, and maintaining the temperature under reduced pressure.

Regarding instant claim 27, the limitation of the amorphous optically active isomer of lansoprazole that does not show a specific peak under an X-ray powder diffraction analysis would have been obvious over the amorphous lansoprazole isomer taught by Fujishima (Page 13, line 30 to Page 14, line 16). One of ordinary skill in the art would find analyzing the resultant lansoprazole isomer under X-ray powder diffraction obvious. Since the amorphous lansoprazole isomer is rendered obvious by Fujishima, the property associated with the amorphous lansoprazole isomer (i.e., not showing a specific peak under an X-ray powder diffraction analysis) would have been obvious. Please see MPEP 2112.01. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present.

Regarding instant claims 28-29, the limitation of the hydrated crystals that show a specific peak under an X-ray powder diffraction analysis would have been obvious over the method of evaporating to dryness a hydrate of R(+)-lansoprazole, as taught by Fujishima (Page 13, line 30 to Page 14, line 16, Page 2, lines 32-34). One of ordinary skill in the art would find analyzing the resultant hydrated crystal of (R)-lansoprazole

under X-ray powder diffraction obvious. Since the hydrated crystal of (R)-lansoprazole is rendered obvious by Fujishima, the property associated with the hydrated crystal of (R)-lansoprazole (i.e., showing a specific peak under an X-ray powder diffraction analysis) would have been obvious. Please see MPEP 2112.01. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. The limitation of drying the hydrated crystals at about 60ºC-70 ºC would have been obvious over the method of producing and drying a hydrate of (R)-lansoprazole, as taught by Fujishima (Page 13, line 30 to Page 14, line 16, Page 2, lines 32-34).

Regarding instant claims 30-31, the limitation of the amorphous optically active isomer of lansoprazole that contains more amorphous form than crystalline form would have been obvious over the amorphous (R)-lansoprazole and the hydrated crystal of (R)-lansoprazole taught by Fujishima (Page 13, line 30 to Page 14, line 16 and Page 2, lines 32-34). One of ordinary skill in the art would find it obvious to modify the drying steps to increase crystalline lansoprazole or increase the amorphous lansoprazole formation.

Response to Arguments

10. Applicant's arguments, see Page 5, filed 08/24/09, with respect to the rejection of claims 23-26 under 35 USC § 103(a) as being unpatentable over Fujishima et al. (WO 00/78745) have been fully considered but are not persuasive.

Applicant argues that contrary to the rejection's position, Fujishima is far from teaching that their crystal of R(+)-lansoprazole is the starting material, let alone that the hydrate form of their crystal of R(+)-lansoprazole can be used as the starting material.

Applicant argues that "Fujishima teaches that their targeted product is the crystal of R(+)-lansoprazole, and the starting material used to obtain the crystal of R(+)-lansoprazole is the amorphous R(+)-lansoprazole. On the other hand, the method of claim 23 involves just the opposite. That is, claim 23 involves producing an amorphous optically active isomer of lansoprazole from hydrated crystals of optically active isomer (R-isomer) of lansoprazole."

This is not persuasive because Fujishima teaches the claimed elements of the process of the isolation of (R)-2-[[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridinyl]methyl]sulfinyl]-I H-benzimidazole (R(+)-lansoprazole) where the filtrate was evaporated to dryness to yield R(+)-lansoprazole as an amorphous substance (Page 13, line 30 to Page 14, line 16). Fujishima also teaches that the starting material is a crystal of R(+)-lansoprazole which may be a hydrate (a 0.5 hydrate to 5.0 hydrate) (Page 2, line 32 to Page 3, line 3). Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the method of evaporating a hydrate of R(+)-lansoprazole to dryness, as taught by Fujishima, and perform the drying at a temperature range of about 20 to about 100°C during the process of routine experimentation, and produce the instant invention. Although concentrating to dryness may be difficult to achieve, Fujishima teaches the evaporation of a hydrate of R(+)-lansoprazole to dryness. Therefore, one of ordinary skill in the art

would manipulate the parameters controlling the drying, such as the temperature, during the process of routine experimentation and produce the amorphous R(+)-lansoprazole.

New Claims 27-31

11. Applicant argues that Hashimoto and Fujishima do not teach or suggest the features of claims 27-31.

This is not persuasive because the limitations of new claims 27-31 would have been obvious over the teachings of Hashimoto, since one of ordinary skill in the art would find analyzing the resultant lansoprazole isomer under X-ray powder diffraction obvious. Since the amorphous lansoprazole isomer is rendered obvious by Hashimoto and Fujishima, the property associated with the amorphous lansoprazole isomer (i.e., not showing a specific peak under an X-ray powder diffraction analysis) would have been obvious. Please see MPEP 2112.01. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present.

Conclusion

13. No claims are allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Aradhana Sasan whose telephone number is (571) 272-9022. The examiner can normally be reached Monday to Thursday from 6:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert A. Wax, can be reached at 571-272-0623. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Aradhana Sasan/
Examiner, Art Unit 1615

/Robert A. Wax/
Supervisory Patent Examiner, Art Unit 1615